

Non-specific genital infection in a general practice

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The rising incidence of male urethral infection of uncertain aetiology is at present a major problem. The reported figures for non-gonococcal urethritis in England and Wales increased in the 20 years from 1951 to 1970 by nearly 38,000, most of these cases being of the non-specific variety. There are epidemiological reasons for thinking that non-specific urethritis (NSU) has its counterpart in women as non-specific urogenital infection (King, 1972). For notification purposes, the condition in both sexes is now referred to as non-specific genital infection (NSGI) with, or without, arthritis. In England in 1971 the venereal disease clinic returns for "NSGI without arthritis" totalled 59,023 for men and 13,397 for women (Department of Health and Social Security, 1972).

The difficulty in defining the clinical disorder in women has contributed to the problem (Catterall, 1971; Department of Health and Social Security, 1970; *Brit. med. J.*, 1971a; Nicol, 1971). In venereal disease clinics the diagnosis in women, who usually attend as contacts of men with NSU, is mainly based on:

- (1) Assessment of cervicitis as shown by clinical appearance, an increase in pus cells according to the phase of the menstrual cycle in smears of the cervical secretion, and a cervical cytology report of non-specific inflammation (NSI);
- (2) Microscopical examination of a Gram-stained urethral smear, excess pus cells denoting the presence of urethritis.

NSU is often asymptomatic. Rodin (1971) found that, in eleven out of 88 asymptomatic men, the disease was undetected at the first attendance but was evident when an early morning smear (EMS) was examined. This suggests that the true incidence of NSU is greater than is shown by the returns. It

has also been suggested (*Brit. med. J.*, 1971b) that figures for NSU might be increased by one-seventh if cases treated by general practitioners were taken into account.

Inflammatory disease of the cervix is often seen in the course of routine examination of women in general practice. In the present investigation an attempt has been made to relate this to possible unsuspected NSU in their male consorts. In addition, the effect of the condom in reducing the frequency of NSGI has been studied.

Material and methods

This study was conducted in a predominantly working-class practice in London. During the investigation 325 women were studied; 80 per cent. were in their third or fourth decade and 95 per cent. were married. 98 women (30 per cent.) were examined because they complained of urogenital symptoms; 227 women (70 per cent.) presented without symptoms and were examined routinely, e.g. for post-natal check, contraception, and periodic cervical cytology. Couples, either partner of whom had had systemic antibiotics within 3 months of examination, and pregnant women have been excluded from this report.

When these 325 women were examined, it was explained that tests involving both sexual partners would be done "to exclude inflammation". In every case women were asked about a past history of genital disorders and for details of recent sexual contact and contraceptive technique.

Clinical examination

With the woman in the dorsal position, the external genitalia were examined and cleansed and the vagina and cervix inspected *via* a Cusco's speculum. Specimens were collected as follows:

(1) A scrape from the squamo-columnar junction of the cervix was spread with an Ayre's spatula on a glass slide and fixed for cytology.

(2) Vaginal, cervical, urethral, and rectal specimens were spread on glass slides; further specimens from the vagina, cervix, and occasionally the urethra and rectum

were inoculated on to Bushby's and Sabouraud's culture media, and additional swabs from these sites were put into bottles containing Stuart's transport medium. A bimanual pelvic examination followed to exclude uterine enlargement and adnexal disease, blood was taken to exclude syphilis and, when urinary symptoms were complained of, a mid-stream urine (MSU) was obtained to exclude urinary tract infection.

Early morning urine collection in men

After examination each woman was given two sterile 10 ml. urine containers for her consort with the following instructions:

- (1) They should refrain from intercourse on the night before collection;
- (2) The partner should not take fluids after 7 p.m. and should void urine on retiring;
- (3) Next morning, after cleansing the penis with soap and water, he should pass first and second overnight urine specimens into the bottles provided (labelled 1 and 2).

Microbiological examination

(1) Vaginal swabs in Bushby's medium were kept at 37°C. for prompt wet smear microscopy by the author for *C. albicans* and *T. vaginalis*, and this was repeated for the latter after at least 48 hrs' incubation.

(2) Vaginal material inoculated on to Sabouraud's medium was incubated at 37°C., colonies of *C. albicans* being identified by the author by the "germ tube" technique (Mackenzie, 1962; Mardon, Hurst, and Balish, 1971).

(3) Bottles of Stuart's transport medium containing vaginal, cervical, and sometimes urethral and rectal swabs were sent to Whipps Cross Public Health Laboratory as soon as possible for culture for *N. gonorrhoeae*, *T. vaginalis*, and *C. albicans*.

(4) The slides with smears from the four sites were stained by Gram's method and examined for excess pus cells, *N. gonorrhoeae*, and *C. albicans*.

Recording of results

WOMEN

NSGI was diagnosed in the presence of all the following criteria, with or without the clinical appearance of cervicitis, and/or microscopic urethritis (10 or more pus cells in several high-power fields, magnification $\times 600$):

(a) Fifty or more pus cells in several high-power fields (magnification $\times 600$) of the cervical smear without the above-mentioned specific pathogens (Fig. 1);

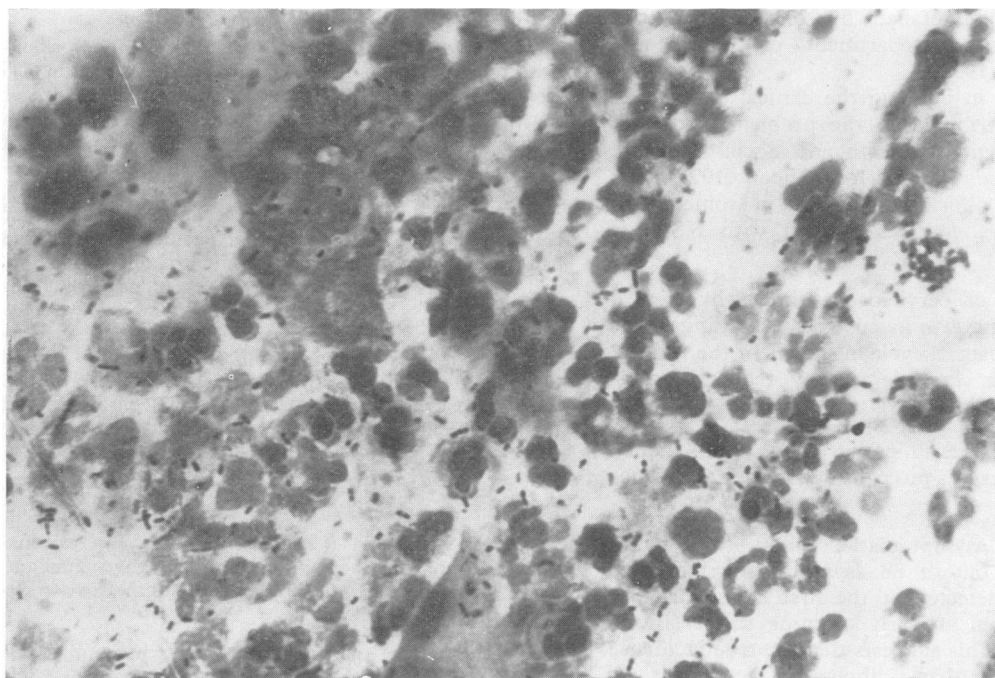


FIG. 1 Gram-stained smear of cervical material ($\times 600$) from an asymptomatic wife, aged 27. The late secretory phase smear shows excess pus cells, many in clumps. The lactobacilli are largely replaced by a coccal flora which did not yield a pathogenic organism on culture (Husband—see Fig. 2)

- (b) Negative cultures for the above pathogens;
- (c) Confirmation of cervical NSI by the cytology laboratory.

The cytological criteria for determining inflammation, more than one of which had to be present, were: presence of pus; nuclear enlargement; changes in the background bacterial pattern to other than lacto-bacilli, *e.g.* cellular debris with coccal organisms; presence of deeper layer cells without other explanation; alteration of staining characteristics (Prendiville, 1973).

MEN

The men investigated were the consorts of the screened women. The urine bottles labelled 1 and 2 contained the first portion of the overnight urine (o/u 1) and MSU specimens respectively. Each specimen was centrifuged at approximately 3,000 r.p.m. for 10 min. on the same day and the wet and dry stained sediment was examined microscopically for the presence of pus cells. If ten or more polymorphs with few organisms were seen in several oil-immersion fields ($\times 1,500$), a diagnosis of urethritis was made (Figs. 2 and 3).

When both samples contained excess polymorphs, the MSU was sent to the local Public Health Laboratory to exclude urinary tract infection. Men with significant pyuria were requested to attend to query the absence of

symptoms and to identify any genital disease; they were asked about recent sexual contact and blood was taken for serological tests for syphilis. In addition, in the cases of those men who were able to attend for an EMS, a urethral swab was taken for culture for *N. gonorrhoeae*, *T. vaginalis*, and *C. albicans*, after subpreputial and meatal cleansing. The urine was then collected and examined for pyuria as described above.

Treatment

Men and women who were found to have NSGI were treated with oxytetracycline tablets 500 mg. four times a day for 2 weeks, with instructions to abstain from sexual intercourse. When re-examination showed that this treatment had not eradicated the infection from either or both of the partners, the woman was referred to a gynaecologist and/or the man was referred to a venereal disease clinic, for further investigation and treatment.

Results

There were no cases of gonorrhoea or syphilis. Sixteen women (4.9 per cent.) were found to have trichomoniasis. Fourteen women (4.3 per cent.) were found to have candidiasis. These thirty

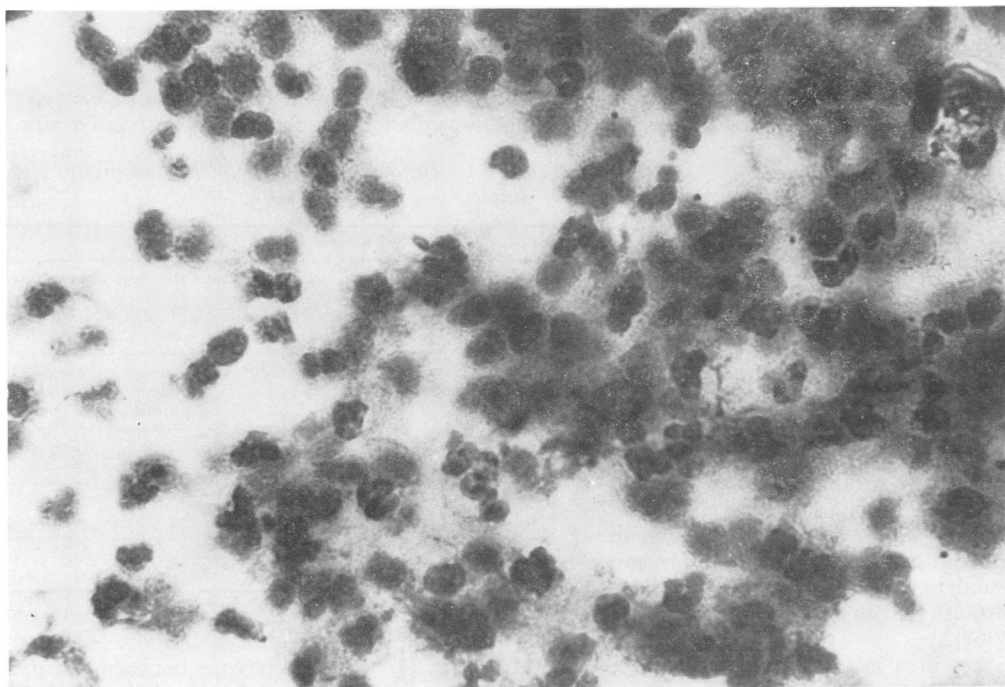


FIG. 2 Gram-stained smear of o/u 1 sediment ($\times 600$) from an asymptomatic husband aged 33. Numerous pus cells are present, indicating a moderately severe degree of NSU; MSU was normal (Wife—see Fig. 1)

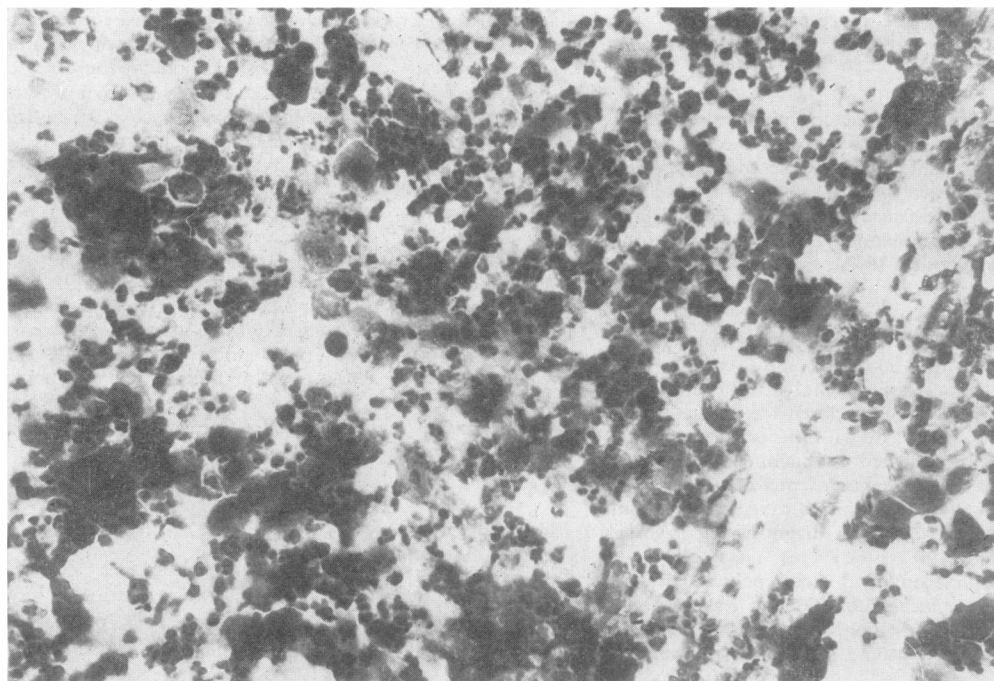


FIG. 3 Gram-stained smear of o/u 1 sediment ($\times 400$) from an asymptomatic man aged 23, whose wife had NSGI. Pus cells are very numerous, indicating a severe degree of NSU. MSU was normal

women have been excluded from the analysis. The remainder were divided into the following groups:

POSITIVE GROUP (I) (182)

A Women with NSGI: male partners with NSU (54)

B Women with NSGI: male partners without NSU (128)

CONTROL GROUP (II) (113)

A Women without NSGI: male partners with NSU (2)

B Women without NSGI: male partners without NSU (111).

Table I compares the four sub groups and shows that, out of 182 couples in which the woman had NSGI, in 54 the man was found to have NSU and there was therefore evidence of a sexually-transmitted disease. On the other hand, out of 113 couples in which the woman did not have NSGI, in only two was the man found to have NSU. The difference was highly significant (χ^2 with 1 degree of freedom = 33.49; $P < 0.00001$).

Of the 54 positive men in Group I A, only three had symptoms and three others had a previous history of NSU; 49 (90 per cent.) of these men were uncircumcised. Of the two positive men in Group II A, neither had symptoms.

The condom proved to be an effective barrier to sexual transmission of infection, because in Groups I

TABLE I *Incidence of NSGI in the four groups of couples*

Sex		Women		Men	
Diagnosis		As worded on cytology form—Non-specific cervical inflammation		By wet smear and Gram-stain of sediment of spun 10 ml. o/u 1 and/or EMS	
Group	No. of couples	More than slight	Slight	Average no. pus cells in several oil-immersion fields ($\times 1,500$)	
				10–20	More than 20
I A	54	44	10	33	21
B	128	93	35	0	0
II A	2	0	0	2	0
B	111	0	0	0	0

B and II A, where NSGI was found in only one partner of each couple, it was much more frequently used (Table II). The difference between the proportion of *positive* men and the proportion of *negative* men who used a sheath when the female partners were positive was highly significant (χ^2 with 1 degree of freedom = 14.63; $P < 0.00014$).

TABLE II Comparison of use of condom in the four groups studied

Group	No. of couples	No. using condom
I A	54	4
B	128	28
II A	2	0
B	111	30

The number of pus cells in several oil-immersion fields ($\times 1,500$) was counted in smears of the centrifuged deposit of both first and second portions of the overnight urine specimens from the men. In one asymptomatic man, excluded from this trial, excess pus cells were found in both specimens and culture showed a coliform urinary tract infection.

Table III shows that, in the 56 men with NSU, the second urine stream was normal; in 239 men without NSU both specimens were normal. Wet and stained smears from the same urinary sediment showed a similar pus count, and also examination of the urine collected at the time of the EMS presented a picture comparable with that shown in the man's previous o/u 1. Six (15 per cent.) of the forty men in Table IV showed more pus cells in the previous o/u 1, while four of the forty men (10 per cent.) showed more pus cells in the second o/u 1. However, in none of these ten men was the discrepancy great enough to alter the grouping in Table I.

TABLE III Comparison of no. of pus cells counted in o/u 1 and MSU in men

No. of men	Average no. of pus cells in several oil-immersion fields ($\times 1,500$) of wet and dry smears of 10 ml. spun urine	
	o/u 1 sediment	MSU sediment
239	<10	<10
32	10-20	<10
24	>20	<10

The efficacy of diagnosis of NSU by microscopic examination of o/u 1 and by EMS is compared in Table IV. Of forty men, 27 showed more pus in the urine while eight showed more in the urethral smear; in five the pus count was equal; in 26 there was an insignificant number of pus cells in the EMS, although the urine showed significant numbers of pus cells, and in eight the reverse was the case (Fig. 4, overleaf).

Effects of treatment

WOMEN

Antibiotic therapy was considered to have been effective when there was reversal of the diagnostic

TABLE IV Comparison of relative value of o/u 1 and EMS in diagnosing NSU in 40 men

No. of men	Average no. of pus cells in several oil-immersion fields ($\times 1,500$)	
	Wet smear and Gram-stained sediment of 10 ml. spun o/u 1	Gram-stained EMS
5	10 to 20	10 to 20
3	>20	<10
1	>20	10 to 20
23	10 to 20	<10
8	<10	10 to 20

criteria for NSGI, especially those based on the cervical cytology. This was the case in 31 (57 per cent.) of the 54 women in Group I A, while the remaining 23 (43 per cent.) were referred to a gynaecologist.

MEN

It was possible to treat 47 of the men in Group I A with oxytetracycline; 29 of them (62 per cent.) showed no pyuria on repeat examination of their early morning urine, although five required more than one course of treatment.

Discussion

The results reported in this study have been arrived at by first screening women and then tracing and examining their male consorts, which is perhaps the reverse procedure to that generally obtaining in clinics (King, 1971); it is postulated that the low-grade recurrent genital infection, found in the woman especially as cervicitis and in the man as asymptomatic NSU, may be passed to and fro at coitus.

Selwyn and Oates (1971) believe that a symptomless carrier state is common in women and that such women constitute the main reservoir of infection of NSGI, and Csonka (1972) has stated that NSU occurs more commonly within marriage than gonorrhoea and may develop after contact with an apparently healthy woman. In the present study, 58 per cent. of women with NSGI presented without symptoms. Nevertheless a complaint of vaginal discharge could in most of these cases be elicited by direct questioning. On examination, cervical discharge appeared to be more profuse and purulent in infected women than in those in the control group.

As screening proceeded, it became apparent that confirmation of NSGI could be obtained by a Gram-stained cervical smear plus cervical cytology in almost all cases in which there was macroscopic cervicitis with or without erosion. Although the role of non-malignant erosion in NSGI is equivocal

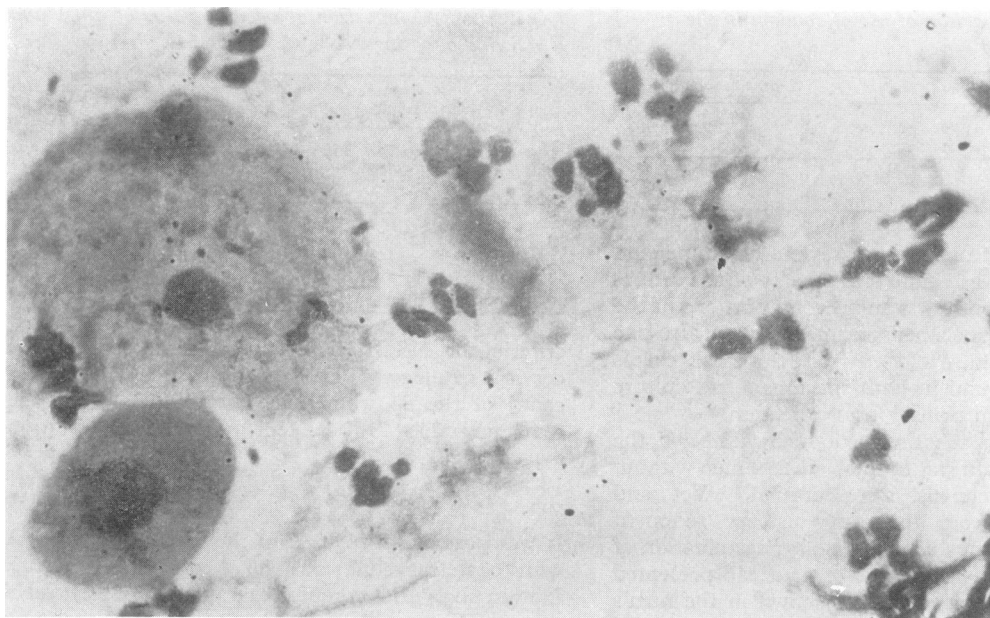


FIG. 4 Gram-stained EMS ($\times 1,500$) from an asymptomatic man aged 39 whose wife had NSGI. More than 10 pus cells were visible in several fields. MSU was normal. The o/u 1 showed less than 10 pus cells per field. $\times 1,500$

and it may not be possible to diagnose it by cytology (Wachtel, 1969), it was thought to be the underlying disease in the 43 per cent. of women whose NSGI did not improve with antibiotic treatment. Recurrence may occur after the surgical treatment of cervical erosion. Possibly this is related to the method used (Barańska, Higier, Jablonski, and Sławinska, 1969; Ostergard, Townsend, and Hirose, 1969), or is due to associated factors, *e.g.* ectropion (Perchard, 1972), and perhaps also to infection from an untreated male partner during healing. It is suggested that, when women with cervicitis are referred for gynaecological treatment, their consorts should be checked for NSU, whether or not they have symptoms.

The results show that, in this general practice, NSU is common in men and is usually asymptomatic. It is readily diagnosed by microscopy of o/u 1, which is a more pleasant and convenient procedure for the patient than an EMS. The latter would help where the diagnosis is in doubt, but examination of three weekly o/u 1 specimens may be preferable. The presence of threads in uncentrifuged urine generally indicated urethritis when they contained many pus cells, but the degree of urinary clarity and the amount of spun sediment are not relevant in diagnosis unless associated with pyuria.

Boyd, Csonka, and Oates (1958), in an investigation of 200 males with NSU, found that 23 per cent. denied extramarital sexual intercourse (EMSI) within the previous 3 months. Recent EMSI did not appear to be prevalent in the present study but, although not investigated here, the possibility of non-recent extramarital and premarital intercourse by one or both partners must be considered when NSGI is found. EMSI was known to have occurred recently in five couples in Group I A.

As regards treatment, it is known that untreated men with NSU gradually recover in most cases, but withholding antibiotics prolongs discomfort and anxiety and increases the risk of complications and spread to others (King, 1964). Attitudes to treating asymptomatic female contacts vary (Csonka, 1972), but most venereologists would give the same course of treatment as that for men, hoping to lessen both the risk of re-infection of the male and of non-specific salpingitis in the female (*Brit. med. J.*, 1971 b).

A good proportion of NSGI seen in this general practice may be similar to that found in venereal disease clinics, but the reason for the relative lack of symptoms in the men is not clear. It may be partly because men with symptoms of NSU commonly attend clinics without first seeing their general practitioner. Also the findings of Rodin (1971) show

that, if all men attending a clinic had EMS examinations, a large number with asymptomatic NSU would be discovered.

The results show that the condom affords protection against the transmission of infection; of the four most widely used methods of contraception (coitus interruptus, condom, IUD, and oral contraceptives), only the condom can prevent 'to and fro' infection.

Conclusion

In this previously undetermined field in family practice, women appear to constitute the main reservoir of genital infection, the diagnosis being substantiated by cervical cytology in every case. The results of the latter in this practice as a whole have revealed that 50 per cent. of women examined have NSI. This fact, taken with the results given here for men, implies that 15 per cent. of the sexually active male population of the practice has NSU.

Verification of these findings is necessary but, if confirmation is forthcoming, it would appear that infection from an apparently innocent regular female partner may be a contributory factor, hitherto underestimated, in NSU.

It may be predicted that chronic latent female genital inflammation will be perpetuated and that the incidence of NSGI will increase, if the protective condom is replaced by contraceptive drugs, the IUD, and vasectomy. This point should be considered when education schemes directed towards the control of sexually-transmitted disease are being formulated.

Summary

The incidence and features of non-specific genital infection as seen in a general practice are discussed, especially in relation to sexually-transmitted disease in the general population.

Of the male partners of 182 women considered to have non-specific genital infection, 54 (30 per cent.) had evidence of non-specific urethritis based on examination of the early morning urine and/or early morning smear; of these, 48 (89 per cent.) were asymptomatic and had no previous history of urethritis. In a control group of 113 women, only two (1.8 per cent.) of their male partners had non-specific urethritis and in both cases this was asymptomatic.

Sexual transmission of infection was significantly reduced by the use of the condom.

I am indebted to Dr. B. T. Thom, formerly Director of the Public Health Laboratory, Whipps Cross Hospital, and now of Brighton Group Hospitals, for his continued support of my studies. I thank Dr. J. T. Prendiville and his cytology staff at Chase Farm Hospital, Dr. A. E. Wilkinson and his staff at the V.D. Reference Laboratory, and those local colleagues who have allowed me to

investigate and treat their patients involved in this study. I am also grateful to Dr. C. S. Nicol, of St. Bartholomew's and St. Thomas' Hospitals, and to Dr. J. D. Oriel, of University College Hospital, for reading the proofs of this paper and advising on aspects of its presentation.

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Infection génitale non spécifique en pratique générale

SOMMAIRE

On discute de l'incidence et des caractéristiques des infections génitales non spécifiques telle les voit le généraliste, ceci spécialement en relation avec les maladies transmises par voie sexuelle dans la population rurale.

Sur les partenaires masculins de 182 femmes considérées comme ayant une infection génitale non spécifique, 54 (30 pour cent) présentaient une uréthrite non spécifique, ceci reposant sur l'examen de l'urine du matin et/ou sur celui de la goutte matinale; parmi eux, 48 (89 pour cent) étaient asymptomatiques et n'avaient aucun antécédent d'uréthrite. Pour un groupe témoin de 113 femmes, deux seulement (1,8 pour cent) de leurs partenaires masculins avaient une uréthrite non spécifique et, dans les deux cas, celle-ci était asymptomatique.

La transmission de l'infection sexuelle fut réduite d'une manière significative par l'emploi du condom.